Mathematical Modelling in Diabetes Mellitus: A Computational Approach

SHORT SYNOPSIS

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Certificate

I hereby declare that the short synopsis "Mathematical Modeling of Diabetes Mellitus": A Computational Approach" being submitted in partial fulfillment of the requirement for the degree of Doctor of Philosophy in Mathematics under SET, of Manav Rachna International Institute of Research & Studies, Faridabad during the academic year 2021-2022. It is an authentic and genuine record of original work carried out under the supervision of Dr. Deepak Kumar and Dr. Richa Gupta that has not been submitted in full or part to any other university or institute for a degree or diploma. Additionally, the short synopsis has been validated to be free of plagiarism, and proof has been provided.

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ABSTRACT

The primary objective of mathematical biology is to apply several applied mathematical techniques and approaches to develop analytical and predictive models of biological processes. This approach uses mathematical models to clarify the diabetes process. Diabetes is a disease of metabolic disorders characterized by high glucose in the patient. Type I and type II diabetes are the two basic forms of the disease and another important form of diabetes is gestational diabetes, which occurs throughout pregnancy. Mathematical models are created that represent the entire diabetes system. The use of mathematical models is becoming more and more crucial in understanding vital actions and processes. The study focusses in the increasing prevalence of diabetes, especially in India, where urbanization and lifestyle changes contribute to the rising incidence.

This study aims to shed information on the various metabolic pathways and biochemical interactions of medicinal plants in the regulation of blood glucose levels, emphasizing their vital involvement in the process. The work clarifies several herbal extracts' efficacy and safety profiles, such as Aloe vera, Garlic, Gurmar, Bitter Melon, Neem, Tulsi, and through a literature review and empirical evidence.

There are so many diseases occur in the human body due to overweight and obesity, one of these is diabetes mellitus. Our upcoming research aim is to form a mathematical model that will describe the effect of overweight and obesity on diabetes mellitus by taking some parameters that are related to body weight.

This work is beneficial in the area of healthcare sciences since it helps manage the rising number of diabetics. It is also easily understood by the average person because of its graphical presentation.

Keeping it under control becomes crucially important. In this field, a significant amount of work is needed.

Key words: Biomathematics, Mathematical Models, Diabetes, Differential Equations, Genetic algorithm.

CONTENTS

S. NO.	CONTENTS	PAGE NO
1	INTRODUCTION	5-6
2	LITERATURE REVIEW	6-9
3	DESCRIPTION OF BROAD AREA	9-11
4	OBJECTIVES OF THE STUDY	11-12
5	METHODOLOGY TO BE ADOPTED	12-14
6	EXPECTED OUTCOME OF THE RESEARCH	14-14
7	REFRENCES	15-18

1. INTRODUCTION

Biomathematics encompasses a wide range of activities at the intersection of the mathematical and biological sciences. It may go by a different name depending on who you speak with some names for it include systems biology, mathematical biology, quantitative biology, or theoretical biology. Depending on who you ask, it may be referred to by a different name.

Developing and applying mathematical frameworks to describe and examine biological phenomena is biomathematics. This frequently entails the examination of biological data, which usually entails combining the models with statistical techniques. Although many of us also employ more statistical models, our models are mechanically driven, which means that their constituent parts represent biological processes (Lee, S. and Clinedinst, L., 2020).

A branch of science called biomathematics studies the various ways that mathematics is used in biology and medicine. The study of biology and medicine is one of the emerging areas for mathematicians. For the mathematician, there are options for engaging in research in this field at all levels of disciplinary. The field of biomathematics is expanding quickly these days and is becoming crucial to the advancement of mathematics in biology and medicine. The biological process is an extremely intricate one. Its characteristics can perhaps be made clearer through mathematical modeling.

Procedures to be adhered to when developing a mathematical model:

1. Recognize the problem to be investigated.
2. Confirm the main parameters.
3. Prepare a mathematical model using these parameters and find the relationship among these parameters.
4. Use various techniques in mathematics to solve the mathematical framework and obtain the findings.
5. Relate these results to a realistic world problem.

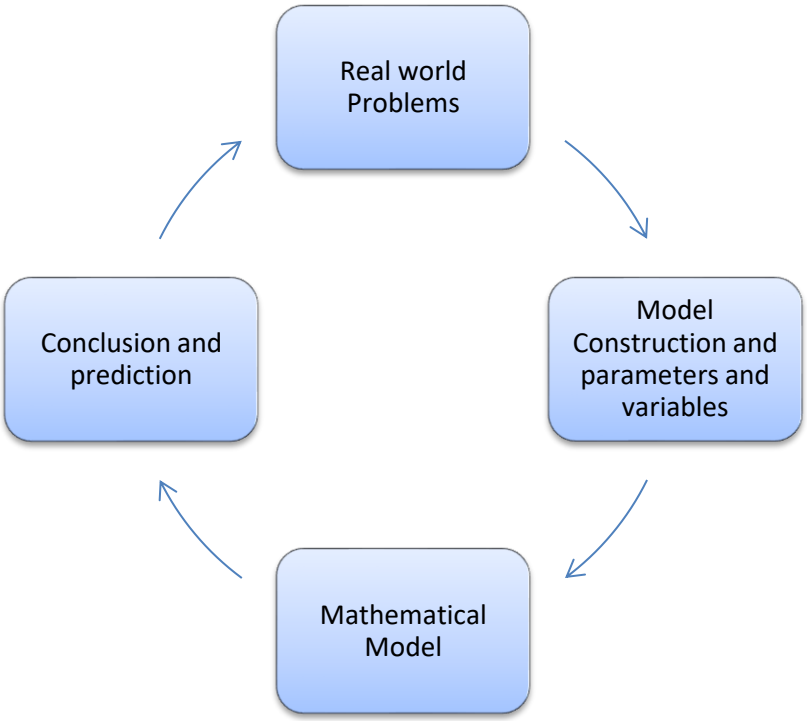

Figure 1: Process of Mathematical Modelling (self)

Elevated levels of blood glucose, or blood sugar, are indicative of diabetes mellitus, a condition that occurs over time. Most occurrences of type 2 diabetes typically occur in older people, which happens when the physical body develops insulin resistance or does not have sufficient insulin production. Common symptoms include excessive dehydration, greater hunger, and an increase in incontinence. Hyperglycaemia that is left untreated can cause several issues.

Diabetic ketoacidosis, a hyperosmolar hyperglycemic condition, or even death are examples of acute consequences. Serious consequences over time include, but are not limited to, cardiovascular illness, stroke, chronic renal disease, ulcers on the feet, harm to the nerves, eye damage, and mental retardation Mathematics is used to define realistic situations. These scenarios provide a foundation for the development of mathematical ideas, methods, and tools. Later on, students can use these contexts to apply their mathematical knowledge, which has subsequently grown less context-specific and more formal and generic (Van Den et.al, 2020).

2. LITERATURE REVIEW

Holland,1973 is credited for sponsoring the original genetic algorithm and is considered the algorithm's father. To effectively solve an issue, Charles Darwin also proposed a random search

strategy for a predetermined search space. This article discusses genetic algorithms, their fundamental workflow, how they operate, and the processes that are involved. Gaetano et. al, 2000 gave a delay differential equation, proven to have positive and limited solutions at all times, and shown to be globally asymptotically stable around a single equilibrium point that corresponds to the pre-bolus conditions.

Dalla Man, et.al in 2007 presented a simulation model diabetes management system, insulin infusion computations, and glucose sensors, for example, a postprandial glucose-insulin system simulation model can be helpful. Here, they create a new simulation model in healthy individuals that depicts the physiological processes that occur after consuming food using the statistical information that has become available in the last few years.

Mathew et.al, 2012 presented a genetic algorithm, The process of evolution had an impact on a group of computer models known as genetic algorithms. These techniques encode a potential resolution to a specific problem on a fundamental data structure that mimics a chromosome, using recombination operators to preserve significant data. Genetic algorithms are commonly considered function optimizers, despite their broad range of applications.

Boutayeb et. al, 2015 presented a model, of the progression of diabetes from its non-complicated state to its complication-ridden state and back again. Three options are put forth based on the expected prevalence of diabetes. Their model demonstrates that optimal control can minimize the total burden of diabetes by limiting the total number of diabetics who experience problems.

Kwach, et.al 2015 presented a mathematical representation of Insulin Therapy in Patients with Diabetes Mellitus is presented in this studyThe system's normal frequency, was determined by analysing its solution. This is the key indicator of the drug's concentration level. It also comprises the external rate of increase in blood glucose, insulin, and adrenaline levels.

Syahputra et.al, 2017 presented a model in which they use the Harris-Benedict equation to determine the number of calories required, and they suggest a genetic algorithm for DM patients' diet scheduling. The findings indicate that the likelihood of fitness score modifications toward the optimal fitness score increases with the number of participants. The World Health Organization (WHO) states that the human body's inadequate consumption of insulin causes type 2 diabetes mellitus (T2DM). Over 95% of diabetics have type 2 diabetes (T2DM), which is mostly brought on by being overweight and sedentary.

Widyaningsih, et.al 2018 gave an SDC (susceptible diabetes complication) Model. The SDC model is a first-order nonlinear differential equation model. The results of the model can be applied to determine how many people are in every section and how those numbers vary over time. The SDC model is used in this work to predict variations in the US diabetes rate. Consequently, the SDC model can accurately forecast the prevalence. The model's parameters were changed to correspond with the average information from an extensive record of healthy individuals who took part in an arrangement involving three tracer meals. With this method, evaluations of the primary insulin and glucose fluxes such as insulin secretion, physiological creation of glucose, glucose utilization, and meal presentation rate were obtained that were essentially independent of the model.

Rosli M., et.al 2020 presented a study in which the paper details the planning and creation of a mobile application for GDM monitoring that makes application of a genetic algorithm to forecast the ideal serving size. To help GDM patients maintain their blood glucose levels during meals, they developed a smartphone application.

Talukder & Hossain, 2020b presented a study in which the research project aims to ascertain the prevalence of diabetes mellitus (DM) and associated risk factors in Bangladesh. The 2011 Bangladesh Demographic and Health Survey provided the pertinent information (BDHS). The Chi-square test was used in bivariate analysis to evaluate the relationship between a few chosen factors and the presence of diabetes.

Kouidere, et.al, 2020 presented a model in which they suggested the best control approach includes educating diabetics about the seriousness of the disease's consequences, the detrimental effects of an unbalanced lifestyle, the environment, treatment options, and psychological aftercare. The optimal controls are characterized by Pontryagin's maximal principle, and the optimality system is solved iteratively. Lastly, using MATLAB, some numerical simulations are run to confirm the theoretical findings.

Dubey and Goswami, 2021 presented a model in which the authors of this work define the fractional model of diabetes and examine the stability of its complications by analyzing fractional operators with exponential kernels. The authors demonstrate the solution's uniqueness and explore the solution's existence using the fixed-point theorem.

Kouidere, et.al, 2021 presented a model in which the study looked at how peer influence affects Fast food intake and the relationship between activity and weight gain to determine the effect that fast food

has on obesity. Two mathematical models were put forth to investigate each component in isolation. Based on their body mass index (BMI), The behavior of persons switching weight classes was portrayed in the models.

Morgan-Benita et.al, 2022 presented a study in which the purpose of this work is to choose metabolites with intelligence features associated with various stages of diabetes using genetic algorithms (GA) and support vector machines (SVMs). This work is innovative in that it suggests a genetic algorithm technique that identifies relevant metabolites at every stage of development, allowing the analysis of which machine learning (ML) model is the most optimal for classifying patients with some stage of T2DM. It was discovered that over 100 metabolites were important at all levels.

3.DESCRIPTION OF BROAD AREA

Diabetes is a metabolic disease that results in increased thirst and huge amounts of urine with high sugar content. There are two kinds of metabolic disorders. Diabetes insipidus is an uncommon metabolic disease characterized by the excessive production of colorless urine with high water content, which results in increased thirst.

Diabetes mellitus is a prerequisite affecting the body's capacity to metabolize carbohydrates. It is brought on by a shortage of the pancreatic hormone insulin, which results in colored urine with high water content, making the patient thirsty. Hyperglycemia in the blood is caused by the buildup of sugar. Numerous conditions, such as physical stress, weight loss, retinopathy, and artery hardening (which causes atherosclerosis), may precipitate the illness. Unoxidized glucose also damages the cells that line blood arteries and other organs. Damage or other areas of the islet cells prevent the cells from secreting insulin, which leads to an underutilization of glucose that results in weight loss, weakness, blindness, polyuria, and neuropathy from the hardening of the arteries. Insulin administration and the distribution of a palatable meal are required for different body frames to maintain the right utilization of insulin for metabolic activities to regulate the proper utilization of blood glucose (Sachan et.al. 2018).

An interesting technique for understanding diseases is a mathematical model. It enhances intuitions, explains formal theory assumptions, estimates parameters, establishes sensitivities, evaluates conjectures, simulates both simple and complicated phenomena, and makes predictions for the future.

Simple and comprehensive models that address many elements of the disease are utilized in the context of diabetes. Simple models typically use a limited number of identifiable parameters, making them insufficient despite their simplicity. Conversely, comprehensive models aim to capture the system by considering all of its interactions.

Diabetes Mellitus:

Type 1 Diabetes Mellitus*:* This arises from damage to the beta cells of the pancreas, that generate insulin. Persons having Type 1 diabetes have insufficient or no insulin production from the pancreas, which prevents sugar from entering the body's cells for utilization as energy. Injections of insulin are necessary for people having Type 1 diabetes to manage their blood sugar concentrations. This type of disease occurs in people that are under age 30.

Type 2 Diabetes Mellitus*:* The pancreas produces insulin in this type of situation, but either insufficient amounts or improper insulin function are produced. Type 2 diabetes affects nine out of ten diabetic patients. This kind primarily affects adults over 40, though it can happen to children as well if certain risk criteria are met. Exercise, weight control, and diet can occasionally be used to manage type 2 diabetes.

Gestational Diabetes Mellitus (GDM): GDM, or gestational diabetes mellitus, is the term used to describe pregnant ladies without previous cases of diabetes that have higher than normal blood glucose rates. What causes gestational diabetes is yet unknown. Pregnancy hormones may be the cause, preventing insulin from acting on its receptors. Cells are unable to adequately absorb glucose as a result. As a result, sugar stays in the blood and keeps rising. Overall Symptoms, Among the common signs of diabetes, are: heightened appetite heightened desire to lose weight hazy vision from frequent urination severe exhaustion sores that refuse to go away (Dwivedi, et.al 2020)

Regardless of wealth, type 2 diabetes has been far more prevalent during the past thirty years in all countries. A long-term illness known as diabetes type 1 occurs when the pancreas produces little or no insulin on its own. It was previously known as insulin-dependent diabetes or juvenile diabetes (WHO). Diabetes modeling is a useful tool for tracking the disease's rising incidence and creating affordable control measures for both the disease's incidence and its effects. (Mohammad, et. al,2023)

Nonlinear differential equation models are very helpful in the treatment of diabetes. These types of models give an idea of the increased no of diabetes and precautions taken after the prevalence of diabetes. Diabetes can be cured by having a proper diet, medication and regular exercise. Mathematical models can give an idea of using medicinal plants in the treatment of diabetes.

RESEARCH GAPS

A broad review of the literature in disclosed that the significant work displayed on diabetes mellitus focuses on mathematical modeling. In the literature review, it is noted that there is a gap for the unfamiliar area of the bio-mathematical model of diabetes mellitus. Past research investigates the area of mathematical theory, which needs to be accomplished with so far not explored areas/matter to improve the field of diabetes mellitus. The gaps noted missed out in earlier research during the work for modeling for diabetes mellitus needs to be filled and the same has been replenished in the current research as described below:

Boutayeb et. al, 2015 Kouidere et. al 2020, presented a model, new mathematical modeling with an optimum control technique for the dynamics of diabetic populations and their complications with the effect of behavioral components, so an improved model for population optimization with a genetic algorithm has been presented in Tyagi, K. et.al,.2022.

Sandhya & Kumar D., 2011, 2016 and 2019 presented a Mathematical Model for the Glucose-Insulin Regulatory System of Diabetes Mellitus with different parameters, so an improved model for population optimization with a genetic algorithm has been presented in Tyagi, K. et. al,.2024. Mathematical modeling has a wide scope in the field of diabetes mellitus, controlling disease, creating awareness among the people to be protected and future prediction and medication.

4. OBJECTIVES OF THE STUDY

From a research perspective, Biomathematics is quite interesting since it has applications in biology and medicine. Using computational modeling, the system of glucose-insulin control and related issues in diabetes mellitus was investigated It is a useful theoretical tool for comprehending the fundamental ideas behind many different ecological and medicinal processes. The major objectives of the study are to find the reason, control complications from the disease, and the impacts of the disease on our society.

The main objectives are

- The overall aim of this study is to understand the determinants of diabetes and the variations in diabetes outcomes and care for people.
- To work on new parameters that affect the mathematical models based on diabetes mellitus.
- To review every study that has previously been conducted in the area of computational models for diabetes mellitus.

- A mathematical model may help to explain a system and to study the effects of different components, and to make useful predictions about behavior.

5.Methodology to be adopted

Building a mathematical model for diabetes mellitus is a challenging task, yet interesting. It has certain steps to construct the mathematical model. These are the following:

a. Identifying the problem of diabetes mellitus and its causes. The important parameters and variables are considered to build a new model for diabetes mellitus disease.
b. After building of a mathematical model, select the solution technique for the problem.
c. To find solutions to the mathematical model through the constraints and problems of the real world.
d. The numerical/authentic data is used to seek the result of the model.
e. The result should be validated with existing standards.

Mathematical Techniques

The following differential equations are being used in the research work:

Mathematical model in Diabetes:

$$\frac{dG}{dt} = -m_1 G - m_2 I + g(t)$$
$$\frac{dI}{dt} = -m_3 G - m_4 I + i(t) \qquad (1)$$

When m_1, m_2, m_3, and $m_4 > 0$ for the following reasons:

1. Excess glucose tends to be absorbed by the liver and tissues, causing $m_1 > 0$.
2. If there is extra insulin, it aids in the tissues' ability to metabolism glucose such that $m_2 > 0$.
3. Extra insulin tends to vanish if there is any, causing $m_3 > 0$.
4. The pancreas is stimulated to release insulin if there is too much glucose, preventing $m_4 > 0$.

Genetic Algorithm

A class of computing models inspired by evolution is known as Genetic Algorithms. Genetic Algorithms are a type of evolutionary-inspired computer models. These techniques encode a suggested fix for a specific problem on a fundamental data structure that mimics a chromosome while preserving relevant data through the use of recombination operators. Genetic algorithms are commonly

considered function optimizers, despite their vast range of applications. (Tyagi et. al, 2024).

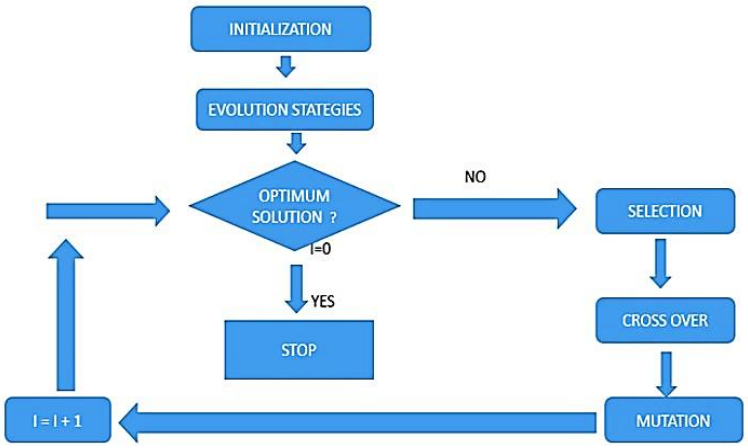

Figure 2: Mechanism of Genetic Algorithm(self)

Table 1: Terminology of Evolutionary Algorithm

Nature	Calculations	Additional details
Population	Set of solutions	the quantity of testable chromosomes
Individual	Solution to a problem	Single solution
Fitness	Standard of a solution	Fitness is calculated for each individual.
Chromosome	Encoding for a solution (strings)	1 1 0 1
Gene	Part of the encoding solution	1 or 0

The genetic algorithm that the late John Holland (known as the father of Genetic Algorithm) developed in the early70s is the one I am talking about. These can be defined as those that are based on population models and artificial neural networks. A straight line that shows how a gas is regulated is briefly explained here (McCall, 2005).

Library visit

- National medical library, AIIMS, Delhi.

- Manav Rachna University, Sector 43, Faridabad

Computer techniques:

- MATLAB
- MATH TYPE

6.Expected outcome of the research:

There are so many theoretical and practical challenges due to the human body's complexity. This study's primary goal is to provide mathematical formalism elements, solutions, and some conceptual frameworks for various diabetes-related models. The goal of the models is to investigate diabetes prevention and control diabetes by applying suitable conceptual and mathematical methods. More specifically, mathematical models for diabetes management will be created. Mathematical models will help understand the disease so that it can be cured and many factors will be defined that affect the disease, parameters will be generated that would be unambiguous for the scientist.

PROPOSED TIME FRAME (GANTT CHART):

Year	Plan of Research Work
1st Year	Course work & Literature Survey
2nd Year	Visit to Hospital/lab for Data Collection & Creating models with different Parameters
3rd Year	Analyzing & Publishing Research Work
4th Year	Thesis Writing and Submission

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Mathematical Modelling of Diabetes Mellitus: A Computational Approach

SHORT SYNOPSIS

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ABSTRACT

The primary objective of mathematical biology is to apply several applied mathematical techniques and approaches to develop analytical and predictive models of biological processes. This approach uses mathematical models to clarify the diabetes process. Diabetes is a disease of metabolic disorders characterized by high glucose in the patient. Type I and type II diabetes are the two basic forms of the disease and another important form of diabetes is gestational diabetes, which occurs throughout pregnancy. Mathematical models are created that represent the entire diabetes system. The use of mathematical models is becoming more and more crucial in understanding vital actions

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